

membered carbocyclic or heterocyclic ring contg. 1 or 2 of N, O and S; R9-R12 = H, NO₂, CF₃, opt. substd. Ph, CN, CO₂R₈, COR₈, C(=S)R₈, C(=NH)R₈, SO₂R₈, halo, 1-8C alkyl, 1-8C alkoxy, thio, 1-8C alkylthio, OH, 1-8C alkanoyl, 1-8C alkanoyloxy or NR₅R₆; or when adjacent R₉+R₁₀ = methylene dioxy; n = 0-3; or NR₅R₆ completes a 3-6C ring opt. contg. 1 of N, O or S; or NR₁R₂ and NR₃R₄ = N=CHR₈, N=C(Me)R₈ or N=C(NH₂)R₈ or complete a 3-6C ring opt. contg. 1 or 2 of O, N or S; or R₁, R₃ = C(=O)R₈, C(O)OR₈, C(=S)R₈, C(=NH)R₈, SO₂R₈ or a gp. of formula (ii); x = 0 or 1; y = 1-3; R₈ = H, opt. NR₅R₆ substd. 1-8C alkyl, 2-8C alkenyl or 2-8C alkynyl, 3-10C cycloalkyl opt. contg. 1 of O, N or S, (i), gp. of formula (iii) or NR₅R₆; Ar, Ar' = Ph, imidazolyl, pyrrolyl, pyridyl, pyrimidyl, benzimidazolyl, benzothienyl, benzofuranyl, indolyl, pyrazinyl, thiazolyl, oxazolyl, isoxazolyl, furanyl, thienyl or naphthyl, all opt. substd. by R₉-R₁₂; provided that when X = N and B = NR₃R₄ then one of R₃ and R₄ is other than H.

USE - (I) are **inhibitors** of protein tyrosine kinase. They are used for treating vascular **smooth muscle** proliferative disease including atherosclerosis and post-surgical **restenosis**, **inhibiting** cell proliferation and migration, treating psoriasis, **inhibiting** epidermal growth factor receptor tyrosine kinase (TK), Erb-B2 or Erb-B3 or **Erb-B4**, TK, protein TK, C-Src TKprV-SrcTK, **inhibiting** basic and/or acidic fibroblast growth factor receptor TK, treating bacterial infections, treating **restenosis** esp. of coronary arteries following balloon angioplasty, **inhibiting stenosis** following organ transplant, **inhibiting** bypass graft **stenosis**, **inhibiting stenosis** following venous graft, **inhibiting restenosis** of peripheral vessels following angioplasty and **inhibiting** platelet-deriv. growth factor receptor TK (all claimed). (I) are also used in treating cancer and leukaemia. The dosage of (I) is 1-100mg/kg/day. The adult dose is 50-800mg/day. A unit dose prepn. contains 0.1-500 (pref. 0.5-100)mg (I). Cpd. may be admin. in single or multiple doses orally parenterally.

Dwg.0/0

FS

CPI

FA

AB; GI; DCN

MC

CPI: B06-D07; B06-D08; B14-A01; B14-D06; B14-F07; B14-N17C

=> d his

(FILE 'HOME' ENTERED AT 08:30:37 ON 21 JAN 2003)
SET COST OFF

FILE 'HCAPLUS' ENTERED AT 08:30:54 ON 21 JAN 2003

	E	ERB
L1	276	S E119
L2	3	S ERB B4
L3	310	S ERBB 4
L4	452	S L1-L3
L5	9	S L4 AND SMOOTH(L)MUSCLE(L)CELL
	E	CELL MIGRATION/CT
L6	4088	S E4-E13
	E	E3+ALL
L7	11558	S E1+NT
	E	E10+ALL
	E	CELL PROLIFERATION/CT
L8	12600	S E4-E10
	E	E3+ALL
L9	49797	S E1+NT
	E	E4+ALL
L10	26908	S E5+NT
	E	E40+ALL

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      E E6+ALL
L11    12675 S E3,E2+NT
L12    54568 S E1+NT
L13    103 S L4 AND L6-L12
L14    26 S L13 AND ANTIBOD?
L15    1 S L5 AND L14
      E RESTENOSIS/CT
      E E3+ALL
L16    2714 S E2,E3
      E STENOSIS/CT
      E E4+ALL
L17    806 S E2
L18    8117 S RESTENOS? OR STENOS?
L19    8 S L4 AND L16-L18
      SEL DN AN 2 7
L20    2 S E1-E6
      SEL DN AN L5 1 8
L21    2 S E7-E12
L22    3 S L15,L20,L21
      E GERRITSEN M/AU
L23    125 S E3,E5,E13,E14
      E SLIWKOWSKI M/AU
L24    80 S E3,E5-E8
      E GENETEC/PA,CS
      E GENETECH
      E GENETECH/PA,CS
      E GENETEC/PA,CS
      E GENENTEC/PA,CS
L25    3390 S E4-E65
L26    31 S L4 AND L23-L25
L27    1 S L22 AND L26
L28    3 S L22,L27
L29    30 S L26 NOT L28
      SEL DN AN L29 3 5 6 10 14 17 21 24
L30    8 S L29 AND E1-E24
L31    11 S L28,L30
L32    11 S L31 AND L1-L31
L33    11 S L32 AND (ANTAGON? OR INHIBIT? OR BLOCK? OR ?MODULAT? OR ?PROL
      E BLOOD VESSEL/CT
L34    15 S E61+NT AND L4
L35    0 S E94+NT AND L4
      E URINARY/CT
L36    30 S E15+NT AND L4
L37    12 S L36 AND BLADDER
L38    12 S BLADDER#/CW AND L4
      E ARTERY/CT
L39    6 S E6-E16 AND L4
L40    2 S E111-E119 AND L4
L41    10 S E110+NT AND L4
      E RESPIRATORY TRACT/CT
L42    4 S E3-E41 AND L4
L43    35 S E3+NT AND L4
      E RECOMBINANT/CT
      E E5+ALL
      E E2+ALL
L44    1 S E3,E2 AND L4
      E FUSION/CT
L45    19 S E25+NT AND L4
L46    70 S L34,L37-L45
L47    24 S L46 AND (?MIGRAT? OR ?PROLIFERAT?)
      SEL DN AN 6 19 20
L48    3 S L47 AND E1-E9
L49    12 S L33,L48

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L50 39 S L46 NOT L47,L49,L5,L14,L19-L22,L28,L31,L32
SEL DN AN 11 24 39
L51 3 S L50 AND E10-E18
L52 15 S L49,L51 AND L1-L51

FILE 'HCAPLUS' ENTERED AT 09:19:43 ON 21 JAN 2003

FILE 'BIOSIS' ENTERED AT 09:20:07 ON 21 JAN 2003

L53 500 S L4
E GERRITSEN M/AU
L54 0 S E3,E5,E15,E16 AND L53
E SLIWKOWSKI M/AU
L55 20 S E3,E5-E7,E9 AND L53
SEL DN AN 3 4 17
L56 2 S L55 AND PATENT/DT
L57 3 S E1-E6
L58 5 S L56,L57
L59 5 S L53-L58 AND L58
L60 8 S L53 AND SMOOTH(L)MUSCLE
L61 433 S L53 (L) RECEPTOR
L62 7 S L61 (L) ANTAGON?
L63 102 S L61 (L) INHIBIT?
L64 4 S L59 AND L60-L63
L65 5 S L59,L64

FILE 'BIOSIS' ENTERED AT 09:29:24 ON 21 JAN 2003

FILE 'MEDLINE' ENTERED AT 09:30:09 ON 21 JAN 2003

L66 354 S L4
E CELL PROLIFERATION/CT
E PROLIFERATION/CT
E CELL MIGRATION/CT
E E5+ALL
L67 4939 S E8
E CELL MIGRATION/CT
E E3+ALL
E E2+ALL
L68 28028 S E4
L69 56516 S E4+NT
L70 167713 S CELL?(L)?PROLIFERAT?
L71 0 S L66 AND L67
L72 14 S L66 AND L68,L69
L73 84 S L66 AND L70
L74 18 S L66 AND CELL?(L)?MIGRAT?
L75 98 S L72-L74
E SMOOTH MUSCLE CELL/CT
E E4+ALL
E E2+ALL
L76 4 S L66 AND E3+NT
L77 0 S L66 AND E13+NT
L78 24 S AI/CT AND L66
SEL DN AN 2 16
L79 2 S L78 AND E1-E6
E RECEPTOR PROTEIN-TYROSINE KINASES/CT
E E3+ALL
L80 375 S E14(L)AI/CT
L81 1 S L80 AND L66
L82 2 S L79,L81 AND L66-L81

FILE 'MEDLINE' ENTERED AT 09:39:06 ON 21 JAN 2003

L83 E GERRITSEN M/AU
0 S E3,E5,E10 AND L66
E SLIWKOWSKI M/AU

L84 18 S E3,E5,E6 AND L66
SEL DN AN 3
L85 1 S E1-E3

FILE 'WPIX' ENTERED AT 09:42:20 ON 21 JAN 2003

L86 40 S (ERBB4 OR ERBB 4 OR ERB B4)/BIX
L87 5 S L86 AND (SMOOTH(L)MUSCL?)/BIX
L88 10 S L86 AND ?STENOS?/BIX
L89 9 S L86 AND A61K039-395/IC,ICM,ICS
L90 6 S L86 AND C07K016/IC,ICM,ICS
L91 13 S L86 AND (B14-H01B OR C14-H01B OR B12-G07 OR C12-G07 OR B14-J0
L92 28 S L86 AND (P520 OR P526 OR P633)/M0,M1,M2,M3,M4,M5,M6
L93 7 S L86 AND (GERRITSEN ? OR SLIWKOWSKI ?)/AU
L94 13 S L86 AND (B04-G01 OR C04-G01 OR B04-G04 OR C04-G04 OR B04-B04C
L95 36 S L87-L94
L96 13 S L94 AND L95
SEL DN AN 1 3 5 6 7 8 11 12
L97 8 S E4-E21
L98 10 S L93,L97
L99 25 S L86,L95 NOT L96-L98
SEL DN AN 8 10 11 12 16 17 19 20 21 22 25
L100 11 S E22-E46
L101 21 S L98,L100
L102 21 S L86-L101 AND L101
L103 21 S L102 AND (ANTI OR ANTIBOD? OR ANTAGON? OR INHIBIT?)

FILE 'WPIX' ENTERED AT 10:18:11 ON 21 JAN 2003

FILE 'DPCI' ENTERED AT 10:19:00 ON 21 JAN 2003
E WO2002018444/PN